Complete Summary

GUIDELINE TITLE

Symptom management in cancer: pain, depression and fatigue.

BIBLIOGRAPHIC SOURCE(S)

Symptom management in cancer: pain, depression, and fatigue. NIH Consens Statement Online 2002 Jul 15-17;19(4):1-29.

GUIDELINE STATUS

This is the current release of the guideline.

* * REGULATORY ALERT * *

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory information has been released.

On April 7, 2005, after concluding that the overall risk versus benefit profile is unfavorable, the FDA requested that Pfizer, Inc voluntarily withdraw Bextra (valdecoxib) from the market. The FDA also asked manufacturers of all marketed prescription nonsteroidal anti-inflammatory drugs (NSAIDs), including Celebrex (celecoxib), a COX-2 selective NSAID, to revise the labeling (package insert) for their products to include a boxed warning and a Medication Guide. Finally, FDA asked manufacturers of non-prescription (over the counter [OTC]) NSAIDs to revise their labeling to include more specific information about the potential gastrointestinal (GI) and cardiovascular (CV) risks, and information to assist consumers in the safe use of the drug. See the FDA Web site for more information.

Subsequently, on June 15, 2005, the FDA requested that sponsors of all non-steroidal anti-inflammatory drugs (NSAID) make labeling changes to their products. FDA recommended proposed labeling for both the prescription and over-the-counter (OTC) NSAIDs and a medication guide for the entire class of prescription products. All sponsors of marketed prescription NSAIDs, including Celebrex (celecoxib), a COX-2 selective NSAID, have been asked to revise the labeling (package insert) for their products to include a boxed warning, highlighting the potential for increased risk of cardiovascular (CV) events and the well described, serious, potential life-threatening gastrointestinal (GI) bleeding associated with their use. FDA regulation 21CFR 208 requires a Medication Guide to be provided with each prescription that is dispensed for products that FDA determines pose a serious and significant public health concern. See the FDA Web site for more information.

Additional Notices

- On July 1, 2005, in response to recent scientific publications that report the possibility of increased risk of suicidal behavior in adults treated with antidepressants, the U.S. Food and Drug Administration (FDA) issued a Public Health Advisory to update patients and healthcare providers with the latest information on this subject. Even before the publication of these recent reports, FDA had already begun the process of reviewing available data to determine whether there is an increased risk of suicidal behavior in adults taking antidepressants. The Agency has asked manufacturers to provide information from their trials using an approach similar to that used in the evaluation of the risk of suicidal behavior in the pediatric population taking antidepressants. This effort will involve hundreds of clinical trials and may take more than a year to complete. See the FDA Web site for more information.
- On December 1, 2005, Amgen, Ortho Biotech and the U.S. Food and Drug Administration (FDA) notified healthcare professionals of revision to the WARNINGS, PRECAUTIONS, ADVERSE REACTIONS, and DOSAGE AND ADMINISTRATION sections of the prescribing information for the following three products (Aranesp, Epogen, Procrit). The revised labeling provides updated safety information on reports of pure red cell aplasia and severe anemia, with or without other cytopenias, associated with neutralizing antibodies to erythropoietin in patients treated with these products. This has been reported predominantly in patients with CRF receiving these products by subcutaneous administration. Recommendations for evaluation and treatment are provided in the new prescribing information. See the FDA Web site for more information regarding Aranesp and Epogen and Procrit.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Pain, depression, and fatigue associated with cancer or its treatment

GUIDELINE CATEGORY

Evaluation
Management
Treatment

CLINICAL SPECIALTY

Family Practice
Internal Medicine
Oncology
Pediatrics
Pharmacology
Psychiatry
Radiation Oncology

INTENDED USERS

Advanced Practice Nurses
Health Care Providers
Patients
Physician Assistants
Physicians
Social Workers

GUIDELINE OBJECTIVE(S)

- To provide health care providers, patients, and the general public with a responsible assessment of currently available data regarding management of cancer symptoms such as pain, depression, and fatigue
- To address the following key questions:
    - What is the occurrence of pain, depression, and fatigue, alone and in combination, in people with cancer?
    - What are the methods used for clinical assessment of these symptoms throughout the course of cancer, and what is the evidence for their reliability and validity in cancer patients?
    - What are the treatments for cancer-related pain, depression, and fatigue, and what is the evidence for their effectiveness?
    - What are the impediments to effective symptom management in people diagnosed with cancer, and what are optimal strategies to overcome these impediments?
    - What are the directions for future research?

TARGET POPULATION

Patients with a diagnosis of cancer who experience pain, depression, or fatigue due to cancer or treatment of cancer

INTERVENTIONS AND PRACTICES CONSIDERED

Evaluation/Clinical Assessment

1. Self-report

2. Questionnaires
3. Assessment of pain:
    - Visual analog or numerical rating of pain (unidimensional measure)
    - Pain severity and impairment due to pain (multidimensional measure)
4. Assessment of depression:
    - Structured instruments vs. symptom scales
    - Diagnostic and Statistical Manual Version IV
    - Patient-related symptom severity scales (i.e., Hospital Anxiety and Depression Scale)
5. Assessment of fatigue
6. Assessment of pain, depression, and fatigue

Management/Treatment

Cancer Pain

1. Three-step analgesic ladder developed by the World Health Organization (WHO):
    - Tier one: Nonsteroidal anti-inflammatory drugs (NSAIDs)
    - Tier two: add a weak opioid to the NSAID
    - Tier three: substitute a strong opioid
2. Adjuvants to relieve neuropathic pain or to treat side effects of opioids
    - Antidepressants
    - Anticonvulsants
    - Psychostimulants
3. External beam radiopathy (localized pain)
4. Bisphosphonates (bone metastases)
5. Radionuclides (refractory bone pain)
6. Neurolytic celiac axis block (intractable localized pain)
7. Chemotherapy
8. Cognitive-behavioral treatments (i.e., hypnosis)
9. Alternative modalities

Depression

1. Antidepressants (selective serotonin reuptake inhibitors [SSRI], tricyclic antidepressants)
2. Cognitive-behavioral or psychosocial interventions

Fatigue

1. Exercise interventions (breast cancer)
2. Epoetin alfa (chemotherapy-related anemia and its related fatigue)

MAJOR OUTCOMES CONSIDERED

- Signs and symptoms
- Reliability and validity of diagnostic instruments

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The Evidence-based Practice Center (EPC) accepted all studies published in English of patients with a diagnosis of cancer who suffered from pain, depression, or fatigue due to cancer or treatment of cancer. It placed no restrictions on the patients' age, gender, ethnicity, level of advancement of the primary disease (staging), or presence of metastases. The conference planning committee was interested in covering the full trajectory of disease, including but not limited to, periods of active treatment and end of life.

Literature Search

Literature searches were conducted to identify studies published between 1966 and 2001 in MEDLINE®, CANCERLIT®, and the Cochrane Controlled Trials Registry. For cancer pain, the EPC applied the same search strategy used in its previously published Management of Cancer Pain evidence report to identify new studies published in the period from December 1998 through June 2001. The National Library of Medicine, as a partner in the National Institute of Health (NIH) Consensus Development Conference process, with input from the EPC staff, performed the literature search for cancer-related depression and cancer-related fatigue. The searches were supplemented with reviews of bibliography of selected references. The EPC also identified published meta-analyses and used their data for selected topics.

Study Selection

Only studies that assessed the prevalence of the symptom as the primary purpose of the study were used for estimating the prevalence of cancer-related symptoms. For assessment, both retrospective and prospective studies were used, as well as randomized and nonrandomized trials, and cross-sectional and longitudinal studies. Randomized controlled trials were used to analyze efficacy of interventions.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Evidence was summarized using three complementary approaches. Evidence tables provided detailed information about the characteristics and outcomes of all the studies examined. Information from the evidence tables was synthesized into summary tables describing the findings of each study. A narrative description of the studies along with an evidence-grading scheme accompanied the summary table.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus (Consensus Development Conference)

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The National Institutes of Health (NIH) State-of-the-Science Conference on Symptoms Management in Cancer Pain, Depression, and Fatigue was convened on July 15-17, 2002. Participants included a non-Federal, non-advocate, 13-member panel representing the fields of psychiatry, nursing, social work, medical oncology, pediatric oncology, epidemiology, pharmacology, radiation oncology, and the public. In addition, experts in these same fields presented data to the panel and to a conference audience of approximately 300.

Answering predefined questions, the panel drafted a statement based on the scientific evidence presented in open forum and the scientific literature. The draft statement was read in its entirety on the final day of the conference and circulated to the audience for comment. The panel then met in executive session to consider the comments received and released a revised statement at the end of the conference.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The draft statement was read in its entirety on the final day of the conference and circulated to the audience for comment. The panel then met in executive session to consider the comments received and released a revised statement at the end of the conference. The statement was made available on the World Wide Web at http://consensus.nih.gov immediately after the conference.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Conclusions

- Too many cancer patients with pain, depression, and fatigue receive inadequate treatment for their symptoms.
- Clinicians should use brief assessment tools routinely to ask patients about pain, depression, and fatigue and to initiate evidence-based treatments.
- Current evidence to support the concept of cancer symptoms clusters is insufficient, and additional theoretically driven research is warranted.
- Research is needed on the definition, occurrence, assessment, and treatment of pain, depression, and fatigue, alone and together through adequately funded prospective studies.
- Fear of cancer and its consequences must be ameliorated. All patients with cancer should have optimal symptom control from diagnosis throughout the course of illness, irrespective of personal and cultural characteristics.
- The state of the science in cancer symptom management should be reassessed periodically.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

Evidence included presentations by experts; a systematic review of the medical literature provided by the Agency for Healthcare Research and Quality; and an extensive bibliography of cancer symptom management research papers, prepared by the National Library of Medicine. Scientific evidence was given precedence over clinical anecdotal experience.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate evaluation and treatment of pain, depression, and fatigue in cancer patients

POTENTIAL HARMS

All analgesics are associated with potential untoward side effects. Acetaminophen is associated with liver toxicity. Nonsteroidal anti-inflammatory drugs (NSAIDs) may cause stomach irritation, nausea, and bleeding. Opioids are associated with sedation, fatigue, nausea, vomiting, confusion, constipation, urinary retention, sexual dysfunction, itching, sleep disturbances, and dry mouth. Tolerance may necessitate dose escalation.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- The statement reflects the panel's assessment of medical knowledge available at the time the statement was written. Thus, it provides a "snapshot in time" of the state of knowledge on the conference topic. When reading the statement, keep in mind that new knowledge is inevitably accumulating through medical research.
- This statement is an independent report of the panel and is not a policy statement of the National Institute of Health (NIH) or the Federal Government.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

The most commonly described strategy for improving symptom management in cancer patients involves a regular assessment of symptoms using a visual analog scale or numerical rating scales, followed by continuous quality improvement interventions to manage the identified symptoms. These interventions include educating providers and patients, following treatment algorithms, and regular reassessment and follow-up of symptom scores.

The Joint Commission on Accreditation of Healthcare Organizations' standard requiring that pain be assessed initially and periodically in all hospitalized patients is an example of an effort to foster this type of strategy. A few published studies have shown that this type of routine assessment and treatment can improve short-term pain scores.

Strategies for decreasing system barriers need to be addressed at the national or regional level. The National Cancer Institute and other cancer-related organizations need to take the lead in raising the visibility and priority given to symptom management by substantially increased funding and by education of providers and the public. Regulatory barriers need to be revised to maximize convenience, benefit, and compliance and to minimize cost and narcotic diversion for illegal purposes. All prescriptions of opioids for cancer patients should be refillable with proper verification. Pharmacies need to stock an appropriate array

of products to meet the need of patients and providers. Barriers, such as triplicate prescriptions, should be proven for efficacy to prevent fraud or discontinued for cancer patients. Payers for health care need to reimburse adequately for symptom management and medications.

All patients should have access to adequate and timely pain control. Education and awareness of the need for adequate pain management are necessary first steps. Optimal pain relief for cancer patients needs to be a minimally accepted standard. Inadequately treated pain can be considered one indicator of poor quality of care. Survivors, their families, and the community for cancer advocacy represent a core network that may help move these policies forward.

IMPLEMENTATION TOOLS

Resources
Staff Training/Competency Material

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

End of Life Care
Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Symptom management in cancer: pain, depression, and fatigue. NIH Consens Statement Online 2002 Jul 15-17;19(4):1-29.

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2002 Jul 17

GUIDELINE DEVELOPER(S)

National Institutes of Health (NIH) Consensus Development Panel on Symptom Management in Cancer: Pain, Depression, and Fatigue - Independent Expert Panel

SOURCE(S) OF FUNDING

United States Government

GUIDELINE COMMITTEE

National Institutes of Health (NIH) Consensus Development Panel

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

All of the panelists who participated in this conference and contributed to the writing of this statement were identified as having no financial or scientific conflict of interest, and all signed forms attesting to this fact.

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available from the National Institutes of Health (NIH) Consensus Development Conference Program Web Site.

Print copies: Available from the NIH Consensus Development Program Information Center, PO Box 2577, Kensington, MD 20891; Toll free phone (in U.S.), 1-888-NIH-CONSENSUS (1-888-644-2667); autofax (in U.S.), 1-888-NIH-CONSENSUS (1-888-644-2667); e-mail: consensus_statements@mail.nih.gov.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Management of cancer symptoms: pain, depression, and fatigue. Evidence Report/Technology Assessment: No. 61 AHRQ Publication No. 02-E031. Rockville, MD: Agency for Healthcare Research and Quality. July 2002. Available from the AHRQ Web Site.
- CME Material. Symptom management in cancer: pain, depression and fatigue. 2003 Oct 15. Available from the National Institutes of Health (NIH) Consensus Development Conference Program Web Site.

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on January 10, 2005. This summary was updated on May 3, 2005 following the withdrawal of Bextra (valdecoxib) from the market and the release of heightened warnings for Celebrex (celecoxib) and other nonselective nonsteroidal anti-inflammatory drugs (NSAIDs). This summary was updated by ECRI on June 16, 2005, following the U.S. Food and Drug Administration advisory on COX-2 selective and non-selective non-steroidal anti-inflammatory drugs (NSAIDs). This summary was updated by ECRI on August 15, 2005, following the U.S. Food and Drug Administration advisory on antidepressant medications. This summary was updated by ECRI on December 5, 2005, following the U.S. Food and Drug Administration advisory on Aranesp, Epogen, and Procrit.

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